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THE EFFECT OF REPEATED RESTRICTIONS OF MOTOR ACTIVITY UPON SYSTOLIC BLOOD PRESSURE OF ALBINO RATS

M. Poppei and K. Hecht

Translation of "Der Einfluss einer Wiederholten Bewegungseinschraenkung der Lokomotorischen Reaktion auf den Systolischen Blutdruck von Albinoratten," *Acta Biologica et Medica*, Vol. 27, 1971, pp. 297-306.

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16. Abstract

In 54 male and female albino rats the influence of repeated restrictions of motor activity on systolic blood pressure was examined for seven and a half months. With increasing duration of restraint, blood pressure readings from 114 to 146 torr with a high of 240. Blood pressure remained high for five weeks following the experiment, leading to the inclusion that the effects are chronic.

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THE EFFECT OF REPEATED RESTRICTIONS OF MOTOR ACTIVITY UPON SYSTOLIC BLOOD PRESSURE OF ALBINO RATS

M. Poppei and K. Hecht[1]

The increasing frequency of illnesses of the so-called essential arterial /297* hypertonia, particularly in the highly developed industrial countries, has turned the attention of special research, finding itself confronted with a number of possible etiological factors, more and more to the meaning of the psychoneural aspects.

Thus Lang [1] and v. Eiff [2], among others, perceive the major etiological factor of essential hypertonia illness in overburdening of the emotional sphere, in the predominance of negatively colored emotions and affects, in conflicts, in the disturbance of the organism-environment relationship, and in the influence of stresses. In this regard, Lang points out that such disturbances of higher nerve function play a substantial role not only as casual factors of hypertonia illness but as developmental factors as well.

The search for suitable animal-experimental models which permit the study /298 of the etiological and pathogenetic mechanisms and whose objective is to produce results serving the clarification of the human clinical picture is thus a preeminent problem for hypertonia research. Experimentally induced neural disturbances (neurosis, hyperirritation) resulted for the most part in labile and temporary occurrences of hypertonia [3-9 and others]. There were also reports, however, covering the results of relatively constant experimentally induced hypertensive reactions; e.g., von Kreher and Nitschkoff [10], Hecht and Treptow [11], Choinowski and Hecht [12] using rats; by Gnuechtel et al. [13] and Havlicek [9] using dogs, as well as Starzew et al. [16] using apes.

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[1]With technical assistance by R. Geppert

*Numbers in the margin indicate pagination in the foreign text.

Pertinent literature conveys the impression that primates are the most suitable animals on which to study the significance of psychoneural factors for the origin and development of blood pressure failures. Experiments with apes, however, have the disadvantage of a large expenditure in the experiment -- both in the maintenance and resulting limited number of experimental animal -- which impedes statistical processing and a general statement. It is therefore necessary to conduct generally oriented preliminary experiments on laboratory animals, using these results on the primates to work out the experimental details.

Restriction of motor activity had until now received little attention in experimental hypertonia research. Research on the effect of fettering animals has shown that variations of the visceral functional span can be produced. This knowledge was garnered among others by Roessel [17], Hirsch and Reinbach [18], Loewy and Rosenberg [19], Morita [20] from glycemic regulatory processes, by Macho et al. [21] from alterations of the metabolism of the tissue of rats, by Bonfils [22] from the development of ulcers and by the Selye panel [23-26] from the problem of resistance and decussated resistance. These cases were concerned with fettering of short duration whereby the visceral alterations were largely reversible.

Referring to these findings, we established our objective to investigate the effect of frequent repeated limitations of motor activity on the regulation of blood pressure of albino rats, in order to contribute to the clarification of the etiopathogenic mechanisms of hypertonia illness.

Methodology

The experiments were conducted on a total of 54 male and female albino rats. Maintenance and feeding were constant. A control group living under the same conditions, of the same age and sex was attached to each experimental group.

The immobilization method was intended to bring about a limitation of motor activity, but by no means a fettering. /299

We confined the animals in folding plastic tubes corresponding to their body measurements. We took care that the animals in these tubes could assume

the typical albino rat squatting position. Moreover, free mobility of the head was ensured. In the course of the more than 7.5 months which the experiment lasted immobilization times were alternated with times of free movement inside the maintenance cage which measured 39 × 27 × 25 cm and was occupied by five animals.

The immobilization times were varied, consisting generally of one to twenty hours. The duration and arrangement of the immobilization phases of several weeks and the intervening longer pauses were random (Figures 1 and 4).

The bloodless systolic blood pressure measurement was taken at least four hours after the individual immobilization times. In this way the acute effect could be eliminated as much as possible and the possible chronic effects measured.

For the blood pressure measurement, during which the animal was in a small box, a total body warming resulted. The width of the cuff was 12 mm. The pressure was measured 1 cm from the root of the tail.

Results

In the course of the 7.5-month experiment, blood pressure measurements of the experimental animals showed constantly deviations of the systolic blood pressure not observed in the corresponding control group. Apart from minor fluctuations, the latter displayed a constant standard ($\bar{\chi}$ = 114 ± 8 Torr). The burden effect is shown in the mean value curve of one of the animal collectives submitted to repeated immobilization (Figure 1).

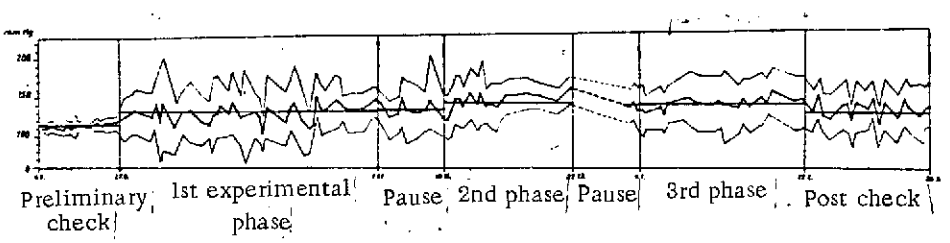

Figure 1. Blood Pressure Chronological Curve of a Group of 18 Animals (middle curve) With Extent of Dispersion Drawn in (upper and lower curve) and the Intermediate Mean Values (horizontal lines).

The blood pressure began to deviate from the beginning of the immobilization burden, a condition which increased as the experiment progressed. In the first test phase of 66 days a high of 135 Torr was observed for the entire stage. The mean starting value was 114 Torr.

In the following 18-day pause the mean value climbed insignificantly to 137 Torr. Throughout the renewed burden period (second experimental phase, 33 days) an increase in blood pressure to 146 Torr was reached whereby an average increase of 32 Torr occurred. In order to check the permanence of the /300
increase in blood pressure, a 15-day absolute pause was inserted. As the subsequent measurements showed the blood pressure increase remained after this phase too, and in the following third burden phase of 43 days. In the post check period of more than five weeks the hypertonic blood pressure deviations remained irreversible (134 Torr).

In contrast to the checks and preliminary checks of the experimental animals the dispersions under stress are more pronounced and stronger at the beginning of the phases than at the end. These dispersions are conditioned by the individual blood pressure chronological curves (Figure 2). Several animals reacted immediately to the immobilization with a high increase of the systolic blood pressure -- individual values of up to 240 Torr were observed -- others showed negligible increases and in the case of still others the increase in blood pressure occurred only after an initial drop in blood pressure.

These results permit the conclusion that the observed blood pressure deviations represent a chronic effect. In order to check the replicability of the chronologized increases in systolic blood pressure occasioned by repeated immobilization, the experimental arrangement was varied so that in the case of two further groups the preliminary check period was lengthened and the test and rest phases were conducted at intervals other than those used in the first experimental series.

The results are presented semi-schematically in Figure 3. In these variations as well blood pressure experienced an increase from the beginning of the repeated immobilization throughout the entire duration of the experiment, which was evident during the stress phases as well as in the rest and post check phases.

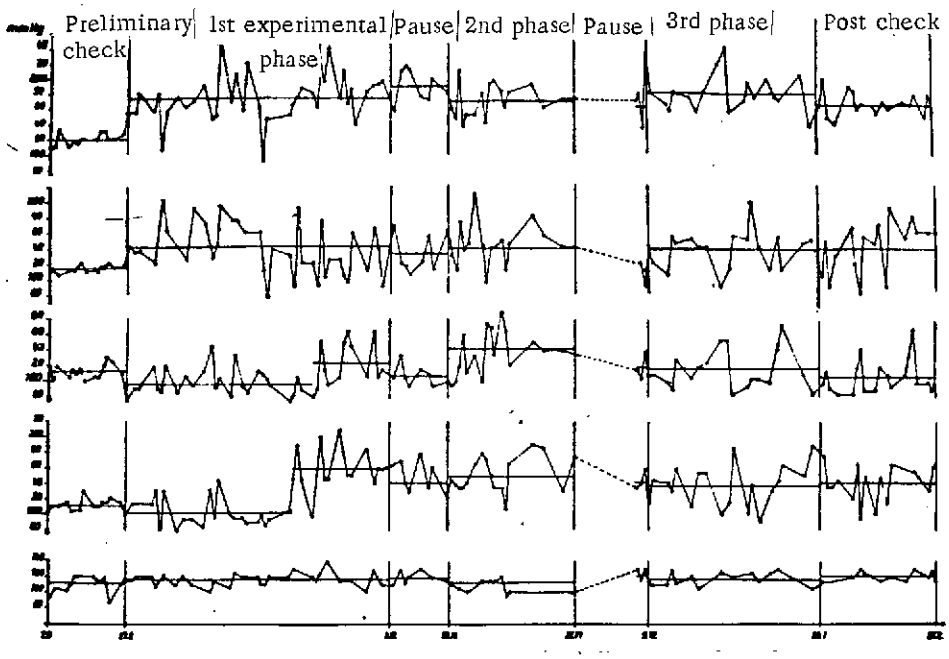

Figure 2. Blood Pressure Chronological Curves of Individual Animals. Horizontal lines equal the mean values over the time; lower curve equals the control.

There was still the question whether the frequency or duration of the individual immobilizations represented the essential factor for the blood pressure deviation. To this end, in the initial stage (25 days) of the first stress phase we investigated the relationships between the mean percentile portion of the duration (100% equals 24 hours) and the mean frequency (100 equals 25 days) of the individual immobilizations on the one hand and the deviation of the blood pressure on the other.

The strongest influence on the blood pressure regulation appeared when the individual immobilizations were of relatively long duration (66% of 24 hours) and when a relatively frequent application (59% of 25 days) of these longer immobilizations occurred during the first stress phase. /302

The blood pressure deviations were on the other hand not so intensive when the immobilizations occurred with less frequency (40% of 25 days) and longer duration (70% of 24 hours) or of shorter duration (25% of 24 hours) and more frequently (56% of 25 days) than in the preceding series.

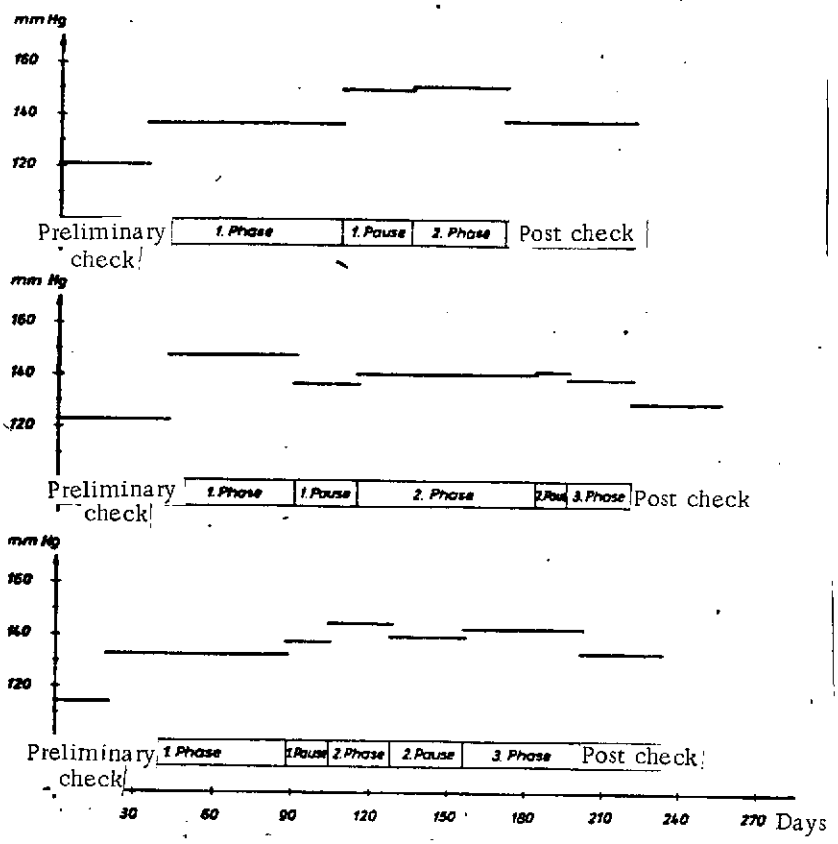

Figure 3. Semi-schematic Representation of Blood Pressure Progress (Intermediate Average) of 3 Animal Collectives.

These results show that the consequences of stress must be viewed in close relationship to the quality and quantity of the burdening factors.

Discussion

Our results show that over a rather long period of time repeated periods of immobilization occurring at random intervals of differing duration which bring about the limitation of the motor activity of the very active laboratory rat led in the course of 7.5 months to chronic hypertonic deviations of the systolic blood pressure. These chronologized hypertonic reactions and the substantial deviations of blood pressure values from day to day bring about a pronounced instability of the blood pressure regulation, such as are commonly observed in the prephase of human essential hypertonia and in juvenile hypertonics [27-29]. There is now the question of the pathological mechanism

toward which we might express our ideas. As the chronic disturbance of blood pressure regulation developed, central nervous factors seemed to be involved, /303 since as yet unpublished results of conditioned reflex experiments (conditioned motor protective reflex) indicate, significant impairment of the central nervous regulation appear during the first stress days. This result can be compared with findings by Herb [30] and Lilly[31] which they disclosed in humans during experiments with reduced afferentation (including that of proprioreceptors). These authors determined that only a few hours of limited mobility and reduced afferentation can lead to severe disturbances of the central nervous processes up to and including hallucinations. Since in the arrangement of our experiment we altered significantly the flow of the reafferentations from the proprioreceptors to the central nervous system, thus provoking an inadequate environment for the animals, the assumption is tempting that the disturbances occurring in the central nervous system are closely related to the disturbed blood pressure regulation. In reaching this conclusion we refer to works by Anochin [32, 33] who considers hypertonia as the result of a continuing "disintegration" of the adaptation mechanisms of the functional system. In electrophysiological tests he determined that the increase in blood pressure leads to an increase in frequency of the impuls salvoes from the aortic nerves to the central nervous system. In the case of sudden jumps the increased impulsation on the part of the aortic nerve appears at differences of 5 Torr; in the case of gradual rises, not until differences of 15-20 Torr. If the increase in blood pressure continues for a long period, the impulsations of the aortic nerve normalize. According to Anochin, an adaptation of the receptors of the "depressor apparatus" occurs in this condition which no longer possesses the capability of producing normal blood pressure conditions.

The areflexia of the carotid sinal zone observed among others by Rajewa [34] in patients in the initial stage of hypertonia illness likewise speaks for the significance of the disturbances of the depressor systems in the development of hypertonia illness.

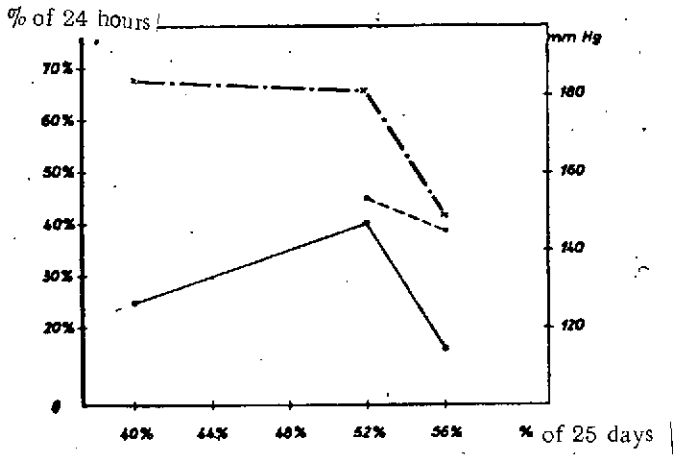

Figure 4. Dependence of Blood Pressure on Duration and Frequency of Immobilization.
—·—·, duration and frequency of immobilization; ----, blood pressure level of a collective of 10 male albino rats; ——, the blood pressure level of a collective of 10 female albino rats

Referring to findings by Anochin and Rajewa as well as to new stress interpretations by Baumann and Graff [35], the following pathological mechanism would be plausible: disturbances in the central nervous regulation occur through the altered re-afference of the proprioreceptors during the immobilization of the animals as in the case of severe irritation. In accordance with the conception by Baumann and Graff the stress increments can affect the blood pressure regulation system and alter the blood pressure level either by way of the neocortical-limbic-hypothalmic-sympathetic or the neocortical-limbic-hypothalamic-hypophysary-corticosuprarenal functional system. The observations that more frequent and longer lasting immobilizations bring on the strongest pathologicals effect leads to the conclusion that in this experimental variation as opposed to others, the compensation mechanisms appear either insignificantly or not al all. Very probably conditioned reflex processes have an effect on the permanence of the hypertensive deviations of arterial pressure. Thus, for example, Havlicek [9] observed blood pressure increases between 20 and 30 Torr, which were statistically significant, in dogs with a conditioned reflex protective dominantas soon as they were brought into the laboratory. The conditioned reflexive replication of hypertensive blood pressure deviations by means of unconditioned stimulus with adrenalin [36] or Renin was of short duration. The constant repetitions of stress, the increasing rise in blood pressure during the experiments, and the evidence of the increased norm during pauses and in the post experimental period make a conditional chronic effect probable. In observing the findings, one must also consider that the disturbance of the

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blood pressure regulation can occur as a result of an interruption of daily rhythm. In support of this assumption is the discovery that the frequent interruptions in normal daily rhythm produce the severest blood pressure changes. This conclusion should be investigated in further experiments.

Histological findings by Eckardt et al., oppose the theory of a possible situationally induced blood pressure increase brought on by the similarity between the immobilization and the measurement boxes. In the case of our laboratory animals they determined changes in the structure and the MPS [Translator's note: expansion unknown] metabolism of the aortic walls which, although comparable qualitatively with those of other blood hypertonic models (renal and docahypertonia) were not so pronouncedly present. Control animals, who were measured in the same boxes, displayed normal histological conditions.

In summary it can be determined that it is possible to induce a chronic deviation of the systolic blood pressure through repeated limitation of motor activity. Included are dependence on the environmental stimulus constellation (quality and quantity of stress), on the inner surroundings of the organism, as well as sex, age, and the individual reactional situation. We will treat the latter question in further works.

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